

## WHAT IS CLAIMED IS:

- But C1*
1. A purified polypeptide characterized as having luciferase activity and a recognition site specifically cleavable by a protease, wherein cleavage results in a decrease in luciferase activity.
  2. The purified polypeptide of claim 1, wherein the luciferase activity is *Renilla* luciferase activity.
  - But C2*
  3. The purified polypeptide of claim 1, wherein the recognition site is a peptide sequence selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.
  4. The purified polypeptide of claim 3, wherein the peptide sequence is substituted for residues 197-200 of SEQ ID NO:2.
  5. The purified polypeptide of claim 1, wherein the polypeptide has a sequence as set forth in SEQ ID NO:4.
  6. The purified polypeptide of claim 1, wherein the protease is a caspase-family protease.
  7. The purified polypeptide of claim 6, wherein the caspase-family protease is selected from the group consisting of a Caspase-3, a Caspase-6, a Caspase-8, and a Caspase-9.
  8. The purified polypeptide of claim 6, wherein the caspase is a Caspase-3.
  9. An isolated polynucleotide encoding the polypeptide of claim 1.
  10. The polynucleotide of claim 9, wherein the polynucleotide has a sequence as set forth in SEQ ID NO:3.
  11. The polynucleotide of claim 9, wherein the polynucleotide encodes a polypeptide that contains a recognition sequence selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.

12. An isolated polynucleotide encoding the polypeptide of claim 5.

13. A polynucleotide encoding SEQ ID NO:2, wherein residues 197-200 of SEQ ID NO:2 are selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.

14. The polynucleotide of claim 9, 10 or 13, wherein T can also be U.

15. A vector containing the polynucleotide of claim 9.

16. The vector of claim 15, wherein the vector is an expression vector.

17. The vector of claim 15, wherein the vector is a plasmid.

18. A host cell containing the vector of claim 15.

19. The host cell of claim 18, wherein the host cell is a prokaryote.

20. The host cell of claim 18, wherein the host cell is a eukaryote.

21. A method of identifying a protease activity modulator, comprising:

contacting a sample containing a protease and a polypeptide characterized as having luciferase activity and a recognition site specifically cleavable by the protease wherein cleavage results in a decrease in luciferase activity, with an agent suspected of modulating the protease activity; and

detecting luciferase activity in the sample before and after contacting with the agent, wherein an change in luciferase activity after contacting with the agent is indicative of an agent that modulates the protease activity.

22. The method of claim 21, wherein the protease is a caspase-family protease.

23. A method of identifying a caspase activity modulator, comprising:

contacting a sample containing a caspase-family protease with an agent suspected of modulating the caspase activity and a polypeptide characterized as having luciferase activity and a cleavage site cleavable by the caspase wherein cleavage of the polypeptide inhibits luciferase activity; and

detecting luciferase activity in the sample before and after contacting with the agent, wherein a change in luciferase activity after contacting with the agent is indicative of an agent that modulates the caspase activity.

24. The method of claim 23, wherein the luciferase activity is *Renilla* luciferase activity.

25. The method of claim 24, wherein the polypeptide contains a peptide sequence selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.

26. The method of claim 25, wherein the peptide sequence is substituted for amino acid residues 197-200 of SEQ ID NO:2.

27. The method of claim 23, wherein the polypeptide has a sequence as set forth in SEQ ID NO:4.

28. The method of claim 23, wherein the caspase is selected from the group consisting of a Caspase-3, a Caspase-6, a Caspase-8, and a Caspase-9.

29. The method of claim 27, wherein the caspase is a Caspase-3.

30. The method of claim 23, wherein the sample is a biological sample.

31. The method of claim 30, wherein the sample contains cells.

32. The method of claim 23, wherein the change is a decrease in luciferase activity.

33. The method of claim 23, wherein the change is an increase in luciferase activity.

34. A method of identifying an inhibitor of apoptosis, comprising:

contacting a sample containing a caspase-family protease with an agent suspected of inhibiting the caspase activity and a polypeptide characterized as having luciferase activity and having a cleavage site cleavable by the caspase, wherein cleavage of the polypeptide inhibits luciferase activity; and

detecting luciferase activity in the sample before and after contacting with the agent wherein an increase in luciferase activity after contacting with the agent is indicative of an agent that inhibits apoptosis.

35. The method of claim 34, wherein the luciferase activity is *Renilla* luciferase activity.

36. The method of claim 35, wherein the polypeptide contains a peptide sequence selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.

37. The method of claim 36, wherein the peptide sequence is substituted for amino acid residues 197-200 of SEQ ID NO:2.

38. The method of claim 34, wherein the polypeptide has a sequence as set forth in SEQ ID NO:4.

39. The method of claim 34, wherein the caspase is selected from the group consisting of a Caspase-3, a Caspase-6, a Caspase-8, and a Caspase-9.

40. The method of claim 38, wherein the caspase is a Caspase-3.

41. The method of claim 34, wherein the sample is a biological sample.

42. The method of claim 41, wherein the sample contains cells.

43. An antibody that specifically binds to the polypeptide of claim 1 or to antigenic fragments thereof.

44. The antibody of claim 43, wherein the antibody is polyclonal.

45. The antibody of claim 43, wherein the antibody is monoclonal.

46. A kit useful for the detection of caspase activity, the kit comprising a carrier means with at least two containers, wherein the first container contains a polypeptide characterized as having luciferase activity and a cleavage site cleavable by a caspase-family protease, wherein cleavage results in a decrease in luciferase activity, and the second container contains coelenterazine.

47. A kit useful for the detection of caspase activity, the kit comprising a carrier means with at least two containers, wherein the first container contains a polynucleotide encoding a polypeptide characterized as having luciferase activity and a cleavage site cleavable by a caspase-family protease, wherein cleavage results in a decrease in luciferase activity, and the second container contains coelenterazine.

48. A method of producing a polypeptide characterized as having luciferase activity and a recognition site specifically cleavable by a protease, comprising culturing the host cell of claim 18 under conditions such that the host cell expresses the polypeptide; and recovering the expressed polypeptide.

49. A fusion protein comprising:

a luciferase polypeptide domain; and

a polypeptide of interest linked to the N-terminal or C-terminal end of the *Renilla* luciferase domain.

50. The fusion protein of claim 49, wherein the luciferase domain has a sequence as set forth in SEQ ID NO:2.

51. The fusion protein of claim 50, wherein the luciferase domain contains a peptide sequence selected from the group consisting of DEVD, VEHD, LETD, LEHD, IEPD, DETD, WEHD, YVAD, VEID, and any combination thereof.

52. The fusion protein of claim 49, wherein the polypeptide of interest is  $\beta$ -galactosidase, GST or lambda cII protein.

53. The fusion protein of claim 49, wherein the polypeptide of interest is an antibody, receptor or receptor ligand.

54. The fusion protein of claim 49, further comprising a linker sequence between the *Renilla* luciferase domain and the polypeptide of interest.

55. A polynucleotide encoding the fusion protein of claim 49.

56. A vector containing the polynucleotide of claim 55.

57. The vector of claim 56, wherein the vector is an expression vector.

58. The vector of claim 56, wherein the vector is a plasmid.

59. A host cell containing the vector of claim 56.

60. A method of producing a fusion protein comprising a luciferase polypeptide and a polypeptide of interest, comprising culturing the host cell of claim 59 under conditions such that the host cell expresses the fusion polypeptide; and recovering the expressed fusion polypeptide.

~~61. A polypeptide, comprising:~~

~~a localization sequence;~~

~~a protease cleavable recognition sequence; and~~

~~a luciferase polypeptide sequence~~

~~wherein the localization sequence is linked to the luciferase polypeptide by the cleavable recognition sequence.~~

62. The polypeptide of claim 61, wherein the localization sequence is a mitochondrial or nuclear localization sequence.

63. The polypeptide of claim 61, wherein the protease cleavable sequence has an amino acid sequence as set forth in the group consisting of SEQ ID Nos: 5 to 29.

64. The polypeptide of claim 61, wherein the luciferase has a polypeptide sequence as set forth in SEQ ID NO:2 or 4.

65. A method for detecting protease activity, comprising:

fractionating a cell containing the polypeptide of claim 61; and

detecting luciferase activity of a cellular fraction;

wherein luciferase activity in a cellular fraction other than a fraction corresponding to the localization sequence is indicative of protease activity.